ABBOTT LABORATORIES

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Ref: **Docket No 2003D-0386 - Draft Guidance for Industry on Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical Current Good Manufacturing Practice**

To Whom it May Concern:

Abbott Laboratories is very pleased to have the opportunity to provide comments on the Draft Guidance for Industry on Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical Current Good Manufacturing Practice published on September 5, 2003 in the *Federal Register*.

We participated in the development of the comments submitted by the PDA and our comments reflect that effort.

We thank the Food and Drug Administration for your consideration of our comments. Should you have any questions, please contact Kathy Wessberg (tel: 847-938-1264, e-mail: kathy.wessberg@abbott.com).

Sincerely,

Richard M. Johnson
Encl: Comments

2003D-0386 C6

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ABBOTT LABORATORIES COMMENTS TO FDA ON

Docket No. 03D-0386

COMMENTS

General Comments:

Assuring Issues Are Raised During an Inspection
The Guidance is very clear in the Agency's expectations that this process does not preclude, eliminate, or diminish the communication of issues between the firm and the inspector during the inspection. However, there may be issues, **not** raised during an inspection, that a firm may want to bring forward as part of the scientific and technical dispute resolution process. Firms should be allowed to appeal as part of the dispute resolution process, if they can provide sound reasons for why this issue was not reviewed during the inspection.

Composition of the Dispute Resolution Panel
Impartiality and broad scientific knowledge must be a cornerstone in determining the selection of the panel. The Dispute Resolution Panel must include panel members outside of the Agency. Impartial expertise can be provided by other knowledgeable experts outside of the Agency.

Disclosure of Information
As part of a response to an inspectional observation in the existing process, companies have provided information that is redacted upon public disclosure. Companies, through the benefit of time and experience, are "calibrated" to know how much and which information to provide and through the benefit of a development of trust, know how the Agency will disseminate the information.

Raising an issue as part of the Tier 1 technical dispute process will, in all likelihood, require more information than normally contained within a response to an inspectional observation submitted to the Agency. Additionally, the Agency will face a difficult decision: how much information to release to sufficiently explain the issue and the decision from the dispute balanced against the need to maintain the confidentiality of the proprietary information.

For an issue to be elevated into the Tier 2 Dispute Resolution Panel, even more detailed information will need to be forwarded by the company to the Agency. Any correspondence between the Agency and the firm will also be subject to disclosure. The confidentiality measures to be employed must be of the highest order and should be discussed between the Agency and the firm. At a minimum, the Agency must afford the company an opportunity to review and first comment regarding what the agency intends to disclose.

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Pending Regulatory Action during Interim Periods

It seems inappropriate to take regulatory action while the dispute resolution process is underway. However, it is understandable there may be rare cases, in the interest of public health, where prompt regulatory action is necessary. While there is a pending dispute resolution, the Guidance should clarify the conditions under which the Agency will forestall regulatory action and clarify the conditions under which the Agency will proceed with further regulatory action.

Timing

There is a lack of consistency in time frames as specified in the Guidance. The Agency has stated it has "generally thirty days" to respond to the firm if the Agency disagrees with the firm's request at the Tier 1 level. Further, the Agency can delay a response, albeit with a communication to the firm, without defining a time frame for completion of the request. We suggest that responses from the Agency will be completed in the given thirty days and suggests that in the rare circumstances where additional time is needed, that a maximum time of sixty days be set as the limit.

As an issue progresses into the Tier 2 Process with the need for convening a Dispute Resolution Panel, time frames are not clearly stipulated. Once a determination has been made that an issue warrants review at this level, it will be reviewed at the next meeting for which there is sufficient time on the agenda. The time frame should be more clearly delineated.

The Dispute Resolution Process as a Learning Tool for both the Agency and Industry

The Agency's position on whether the decisions reached by this process will set a precedent for other similar situations should be made clear. We suggest there be a procedure for circulating the information within the Agency as training on the issues and the scientific decisions. Included in this process would be clarification if these decisions effect in practice a change of rules. This can in fact, lead to consistency in the interpretation of regulations by inspectors in the field.

After appropriate redaction, the information from these disputes is invaluable as a learning tool for industry as well.

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Specific Comments:

Lines 19-21

"This document is intended to provide guidance to manufacturers of veterinary and human drugs, including human biological drug products, on how to resolve disputes of scientific and technical issues relating to current good manufacturing practice (CGMP) requirements."

Comments

There is no mention of medical devices (CDRH). Please clarify how the guidance applies to drug/device combination products. E.g., would observations related to QSR interpretation on the device aspects be eligible for the process? Our recommendation is to have this guidance apply to all combination products.

Lines 32-33

"Manufacturers may seek clarification of scientific or technical issues with the inspection team at any time during an inspection."

Comments

We propose to add that a firm can hold a discussion with the relevant FDA Office of Compliance (CBER, CDER) at any time during the inspection to resolve a GMP issue disagreement between the company and inspectors prior to the issuance of a 483 citation concerning the scientific basis for the disputed interpretation of the GMP observation.

Lines 92-96

"At the conclusion of an inspection, investigators usually meet with the manufacturer's management to again discuss observations and solicit views and additional relevant information. These processes are described in detail in the Investigations Operations Manual (IOM) Sections 512 and 516, as listed in Section I of this document."

Comments

Replace "usually" with "are obligated by agency policy to offer to".

Lines 152-155

"The ORA unit will issue a written response to the manufacturer within 30 days of receipt of the request, noting its agreement with the manufacturer and resolution of the dispute. The resolution may take the form of a letter. It may also take the form of an addendum to the existing Form FDA 483.""

Comments

Change " it may also take the form of an addendum to the existing Form FDA 483" to "Any such written response will be considered to be an addendum to the 483, and shall be publicly disclosed, with appropriate redacting, in the event of any disclosure."

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Lines 157-158
"All disputes resolved at the ORA level will be copied to the relevant program center for information and public dissemination."
Comments
Add after public dissemination "with appropriate redaction, in accordance with applicable requirements."

Line 186
"The DR Panel resides at the Agency level."
Comment
Clarify at which level in the Agency the DR Panel resides. We recommend the Agency Level specified is that of the Field Management Team (FMT).

Lines 237-240
"No new information should be submitted as part of a request for formal dispute resolution. If a manufacturer presents new information about an issue in requesting formal dispute resolution, the matter will be returned to the ORA unit for review as appropriate."
Comment
There may be the instance during the inspection where a firm does not understand the investigator's question and therefore not provide information available at the time of inspection. The administrative record will then not contain this information. If in reviewing the observation, the firm understands the observation and realizes that this information would dispute the observation, the firm should have the ability to submit this information as part of their dispute.